## REMARKS

Claims 1-6 and 9 are pending in this application. Applicants herein amend Claims 1, 4 and 5, and cancel Claims 2, 6 and 9. With entry of the amendments, Claims 1-5 are under consideration.

No new matter is added by way of the amendments to the claims. For example, support for fragments of immunoglobulins capable of specific binding to the antigen as recited in claim 1, is found, *e.g.*, on page 4, second paragraph. Support for contacting an antigen and immunoglobulin, wherein the antigen or the immunoglobulin is bound to a solid support as recited in claim 1, is found, *e.g.*, on page 3, fifth paragraph. Support for a basic buffer with a pH between pH 8 and pH 10 as recited in claim 5, is found, *e.g.*, on page 5, last paragraph.

In accordance with the Examiner's instructions, Applicants have amended the specification by adding a claim to the Great Britain priority application. Applicants also have amended the specification to insert trademark indications, as instructed by the Examiner.

Applicants submit herewith copies of the foreign patents and publications cited in the Information Disclosure form and Form 1449 submitted on April 22, 2005. A copy of the previously submitted IDS and Form 1449 is also submitted, along with the requisite fees for consideration.

Amended page 1, attached hereto as an appendix, displays the page number, and reflects the amended title.

Remedy of the objections to the claims

Applicants amend Claims 4 and 5 to recite "bovine serum albumin," as requested by the Examiner. No change in scope or meaning is intended by way of this amendment, which is submitted solely to define the abbreviation "BSA" according to common understanding in the art, as defined on page 5 of the instant specification.

Claims 1-6 and 9 are not indefinite

Claims 1-6 and 9 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

A. The Examiner alleges that the term "fragment thereof" is indefinite. Applicants submit amendments herein clarifying that the fragment is capable of specific binding to the antigen. To the extent that the Examiner maintains the rejection with respect to the amended claim, Applicants traverse. Immunoglobulin fragments capable of specific antigen binding are well-known in the art, and include Fv, Fab fragments, $F(Ab')_2$ fragments, single chain antibodies, and the like. It would be readily apparent to any one of ordinary skill in the art that the fragment of an immunoglobulin to be used in the claimed method should retain the ability to specifically bind the antigen, and which fragments would do so. Accordingly, the claims are not indefinite, and this rejection should be withdrawn.

B. The Examiner alleges that the term "in the *context* of a solid support" is vague and indefinite. Applicants amend the claims herein to clarify that either the antigen or the immunoglobulin is bound to a solid support. Applicants believe that these amendments render this reason for rejection moot.

C. The Examiner alleges that claim 5 is indefinite due to the use of the term "about," in reference to a recited pH, and in reference to a percentage of BSA. Applicants respectfully traverse the rejection on the grounds that any one of ordinary skill in the art would be well aware of the meaning of "about," as directed in the subject disclosure in the context of knowledge in the art. Nonetheless, to expedite prosecution, Applicants hereby amend the claim to specify that "about pH 9" is "between pH 8 and pH 10," and to delete the term "about" in reference to "1% bovine serum albumin." Accordingly, this reason for rejection is rendered moot.

D. Applicants cancel Claims 6 and 9, rendering this rejection moot.

Claims 1, 3 and 4 are fully enabled

The Examiner rejected Claims 1, 3 and 4 under 35 U.S.C. § 112, first paragraph, alleging that the specification "does not reasonably provide enablement for

any and all immunoglobulins of fragments thereof binding any an all antigens." The Examiner admits that the specification is fully enabling for "an assay method for binding the hepatitis B surface antigen to anti-HBs rabbit polyclonal antiserum." In order to expedite prosecution, Applicants hereby amend the claims to "[a] method for the detection of hepatitis B surface antigen...," expressly reserving the right to prosecute cancelled subject matter in one or more continuation applications. As the presently claimed method detects hepatitis B surface antigen, any rejection based on the nature of the antigen is rendered moot. To the extent that the rejection is maintained with respect to the amended claims on the grounds that "the written description only sets forth a method of detecting a hepatitis B surface antigen...with an anti-HBs rabbit polyclonal antiserum," Applicants traverse.

Any antibody or immunoglobulin that is capable of specific binding to the hepatitis B surface antigen is suitable for use in the claimed methods of detecting hepatitis B surface antigen. Accordingly, the claimed method is not arbitrarily restricted to any specific antiserum or antibody (immunoglobulin). Rather, the amended claims relate to the use of any immunoglobulin preparation, whether polyclonal or monoclonal, that is capable of binding to the hepatitis B surface antigen. The claimed method is exemplified in the specification using an anti-HBs polyclonal antiserum. However, one of ordinary skill in the art would immediately recognize that the salient feature of the antiserum is the presence of one or more different immunoglobulin molecules capable of binding to the hepatitis B surface antigen. Similarly, one of skill in the art would be familiar with the identification and production of both polyclonal antiserum and monoclonal antibodies capable of specific binding to the hepatitis B surface antigen. Indeed, at the time of the filing of the subject application, monoclonal antibodies to Hepatitis B surface antigen epitopes and methods for successfully generating them were known in the art (*see, e.g.*, Jolivet-Reynaud *et al.*, *J. Med. Virol.* 65:241-249 (2001), as well as Yamamoto *et al.*, *Biologicals* 25:373-380 (1997)). Accordingly, in view of the knowledge of one of ordinary skill in the art, the specification provides adequate written description for methods utilizing any immunoglobulin, whether polyclonal or monoclonal, that is capable of specific binding to the hepatitis B surface antigen. Applicants, therefore, respectfully request withdrawal of this rejection of Claims 1, 3 and 4.

Claims 1-5 are Novel and Non-obvious

Claims 1-5 stand rejected as allegedly anticipated and/or rendered obvious by Yamamoto, *et al.*, *Biologicals* 25:373-380 (1997), in some cases in combination with additional references. To the extent that the rejections are maintained with respect to the amended claims, Applicants traverse.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Claim 1, and claims dependent therefrom, involve three sequential steps:

(i) contacting the antigen with an immunoglobulin or fragment thereof capable of specific binding to the antigen in the presence of a basic buffer, wherein the antigen or the immunoglobulin is bound to a solid support, to allow binding of the antigen to the immunoglobulin or fragment thereof;

(ii) adding a blocking agent; and

(iii) detecting the binding of antigen to immunoglobulin.

The claim expressly states that steps i, ii, and iii are carried out sequentially but not necessarily consecutively. The indication that the steps are carried out "sequentially but not necessarily consecutively" is meant to indicate that additional steps can optionally be performed between the stated steps. However, it is intended that a single recited step be performed as a unit, and not further subdivided to create a further sequence of steps. Thus, in step (i), a hepatitis B surface antigen, "in a combination with aluminium hydroxide," and immunoglobulin (or fragment thereof) are contacted *in the presence of a basic buffer*.

In the method described by Yamamoto, "HBsAg of adsorbed vaccine was desorbed from alum-gels, then quantitated ..." page 375, second column, under heading beginning "Desorption of HBsAg from alum-adjuvanted HB vaccines,..." First, hepatitis B surface antigen in a combination with aluminium hydroxide was separated from the combination by desorbing it from the alum gel. Next, following desorption, the separated hepatitis B surface antigen was diluted with a blocking agent: 0.5% casein-PBST. Then, after desorption and blocking the diluted antigen was contacted with an immunoglobulin (either polyclonal anti-serum or monoclonal antibody) capable of binding with hepatitis B surface antigen. Thus, the method

described by Yamamoto differs in at least three fundamental ways from the method of claim 1.

First, Claim 1 involves contacting an antigen that is "in a combination with aluminium hydroxide" (alum) with the antibody. The antigen in Yamamoto is separated from alum prior to contacting; therefore, the antigen is not in combination with aluminium hydroxide when contacted with the immunoglobulin.

Second, Claim 1 involves adding a blocking agent *after* the antigen has been contacted with immunoglobulin. Yamamoto describes adding a blocking agent 0.5% casein-PBST to the antigen *before* it is contacted with the immunoglobulin.

Third, Claim 1 involves contacting the antigen and immunoglobulin in a basic buffer with a pH between pH 8 and pH 10. Yamamoto describes contacting the antigen with the immunoglobulin following two-fold serial dilutions in 0.5% casein-PBST. One of skill in the art would recognize that PBST is a commonly used buffer in the art of ELISA. Although the exact pH of this buffer may vary, it is generally between pH 7.0 and pH 7.5, more typically between pH 7.2 and 7.4. For example, a brief review of more than a dozen references to this buffer in the ELISA art, none indicate a pH above pH 7.5. Thus, one of skill in the art would understand that Yamamoto did not contact the antigen and immunoglobulin in a buffer with a pH between 8 and 10.

Accordingly, Yamamoto simply does not teach the limitations of Claim1, or any of the claims dependent therefrom, and this rejection should be withdrawn.

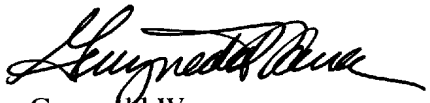
Claim 3 stands rejected as allegedly obvious over Yamamoto in view of Katz, *et al.* (page 103, "*ELISA Technique*"). Katz, *et al.* disclose that an antiserum is placed in microplates, followed by rinsing with PBS and blocking. *After* blocking, the antigen is brought into contact with the immunoglobulin. Further washing is carried out, but no additional blocking is performed. Nowhere does Katze indicate that the antigen and immunoglobulin are contacted in a buffer at pH between 8 and 10. Accordingly, Katz, *et al.* do not remedy the deficiencies of Yamamoto, and this rejection should be withdrawn.

Claims 4 and 5 stand rejected as allegedly obvious over Yamamoto in view of Kono, *et al.* (JP11201970, abstract only). As in the references cited above, Kono, *et al.* describe treating an antigen or antibody with a blocking agent, exemplified by BSA, prior to contacting it with its binding partner (immunoglobulin or antigen, respectively). Nowhere do Kono, *et al.*, indicate the pH at which subsequent contacting is performed. Accordingly, the cited abstract of Kono *et al.*, does not remedy the deficiencies of Yamamoto, and this rejection should be withdrawn.

Conclusion

Applicants respectfully submit that claims 1-5 are allowable in view of the above amendments and remarks. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is requested to call the undersigned at the number below prior to the preparation of any further written action. Applicants reserve the right to prosecute subject matter in the originally filed claims, or any other claims supported by the specification in one or more continuing patent applications.

Respectfully submitted,



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